Clinical trial results:
A Phase 2, Multicenter, Double-Blind, Parallel Group Long Term Extension Study in Rheumatoid Arthritis Subjects Who Have Completed a Preceding Phase 2 Randomized Controlled Trial with ABBV-105 Given Alone or in Combination with Upadacitinib (ABBV-599)

Summary

EudraCT number	2018-002306-31
Trial protocol	BE HU GB ES
Global end of trial date	09 September 2020

Results information

Result version number	v1 (current)
This version publication date	25 August 2021
First version publication date	25 August 2021

Trial information

Trial identification

Sponsor protocol code	M16-763

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03823378
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6-4UB
Public contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 September 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 September 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This was a Phase 2, double-blind, multicenter, long-term extension (LTE) study to assess the safety, tolerability, and efficacy of 3 doses of ABBV-105 (elsubrutinib [ELS] 5 mg, 20 mg, and 60 mg) and ABBV-599 (ELS 60 mg and upadacitinib [UPA] 15 mg) in adults with active rheumatoid arthritis with inadequate response or intolerance to biologic disease-modifying antirheumatic drugs (bDMARDs). Participants who successfully completed treatment in the feeder Study M16-063 (NCT03682705), a Phase 2 dose exploratory study, were eligible to participate in this study. Those who met eligibility criteria and entered this study receiving ELS, ABBV-599, or UPA from Study M16-063 continued on their previously assigned treatment through termination of this study. Participants originally randomized to placebo in Study M16-063 rolled over to ABBV-599 in a blinded fashion in this study.

Protection of trial subjects:

Subjects or their legally authorized representative must have voluntarily signed and dated an informed consent, approved by an independent ethics committee (IEC)/institutional review board (IRB), prior to the initiation of any screening or study-specific procedures.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 May 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	Czechia: 17
Country: Number of subjects enrolled	Hungary: 29
Country: Number of subjects enrolled	Poland: 22
Country: Number of subjects enrolled	Spain: 21
Country: Number of subjects enrolled	United Kingdom: 1
Worldwide total number of subjects	97
EEA total number of subjects	90

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	66
From 65 to 84 years	31
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All randomized participants

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	ABBV-599 in M16-063/ABBV-599 in M16-763

Arm description:

60 mg elsubrutinib capsule once a day by mouth for 48 weeks; 15 mg film-coated upadacitinib tablet once a day by mouth for 48 weeks

Arm type	Experimental
Investigational medicinal product name	Elsubrutinib
Investigational medicinal product code	
Other name	ABBV-105
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Elsubrutinib capsule will be administered orally.

Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	
Other name	ABT-494
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Upadacitinib tablet will be administered orally.

Arm title	ABBV-105 60 mg/UPA placebo

Arm description:

60 mg elsubrutinib capsule once a day by mouth for 48 weeks; placebo film-coated tablet for upadacitinib once a day by mouth for 48 weeks

Arm type	Experimental
Investigational medicinal product name	Elsubrutinib
Investigational medicinal product code	
Other name	ABBV-105
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Elsubrutinib capsule will be administered orally.

Investigational medicinal product name	Placebo for upadacitinib
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Upadacitinib placebo tablet will be administered orally.

Arm title	ABBV-105 20 mg/UPA placebo

Arm description:

20 mg elsubrutinib capsule once a day by mouth for 48 weeks; placebo film-coated tablet for upadacitinib once a day by mouth for 48 weeks

Arm type	Experimental
Investigational medicinal product name	Elsubrutinib
Investigational medicinal product code	
Other name	ABBV-105
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Elsubrutinib capsule will be administered orally.

Investigational medicinal product name	Placebo for upadacitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Upadacitinib placebo tablet will be administered orally.

Arm title	ABBV-105 5 mg/UPA placebo

Arm description:

5 mg elsubrutinib capsule once a day by mouth for 48 weeks; placebo film-coated tablet for upadacitinib once a day by mouth for 48 weeks

Arm type	Experimental
Investigational medicinal product name	Elsubrutinib
Investigational medicinal product code	
Other name	ABBV-105
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Elsubrutinib capsule will be administered orally.

Investigational medicinal product name	Placebo for upadacitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Upadacitinib placebo tablet will be administered orally.

Arm title	UPA 15 mg/ABBV-105 placebo

Arm description:

15 mg film-coated upadacitinib tablet once a day by mouth for 48 weeks; placebo capsule for elsubrutinib once a day by mouth for 48 weeks

Arm type	Experimental

Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	
Other name	ABT-494
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Upadacitinib tablet will be administered orally.

Investigational medicinal product name	Placebo for elsubrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo capsule for elsubrutinib will be administered orally.

Arm title	Placebo in M16-063/ABBV-599 in M16-763

Arm description:

Placebo in M16-063; 60 mg elsubrutinib capsule once a day by mouth for 48 weeks and 15 mg film-coated upadacitinib tablet once a day by mouth for 48 weeks in M16-763

Arm type	Experimental
Investigational medicinal product name	Elsubrutinib
Investigational medicinal product code	
Other name	ABBV-105
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Elsubrutinib capsule will be administered orally.

Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	
Other name	ABT-494
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Upadacitinib tablet will be administered orally.

Number of subjects in period 1	ABBV-599 in M16-063/ABBV-599 in M16-763	ABBV-105 60 mg/UPA placebo	ABBV-105 20 mg/UPA placebo
Started	28	16	12
Completed	7	0	2
Not completed	21	16	10
Adverse event, non-fatal	2	2	-
Other, not specified	19	12	6
Lost to follow-up	-	1	-
Withdrawal by subject	-	1	4

Number of subjects in period 1	ABBV-105 5 mg/UPA placebo	UPA 15 mg/ABBV-105 placebo	Placebo in M16-063/ABBV-599 in M16-763
Started	12	20	9

Completed	2	2	1
Not completed	10	18	8
Adverse event, non-fatal	-	-	-
Other, not specified	8	17	7
Lost to follow-up	-	1	-
Withdrawal by subject	2	-	1

Baseline characteristics

Reporting groups	
Reporting group title	ABBV-599 in M16-063/ABBV-599 in M16-763
Reporting group description:	
60 mg elsubrutinib capsule once a day by mouth for 48 weeks; 15 mg film-coated upadacitinib tablet once a day by mouth for 48 weeks	
Reporting group title	ABBV-105 60 mg/UPA placebo
Reporting group description:	
60 mg elsubrutinib capsule once a day by mouth for 48 weeks; placebo film-coated tablet for upadacitinib once a day by mouth for 48 weeks	
Reporting group title	ABBV-105 20 mg/UPA placebo
Reporting group description:	
20 mg elsubrutinib capsule once a day by mouth for 48 weeks; placebo film-coated tablet for upadacitinib once a day by mouth for 48 weeks	
Reporting group title	ABBV-105 5 mg/UPA placebo
Reporting group description:	
5 mg elsubrutinib capsule once a day by mouth for 48 weeks; placebo film-coated tablet for upadacitinib once a day by mouth for 48 weeks	
Reporting group title	UPA 15 mg/ABBV-105 placebo
Reporting group description:	
15 mg film-coated upadacitinib tablet once a day by mouth for 48 weeks; placebo capsule for elsubrutinib once a day by mouth for 48 weeks	
Reporting group title	Placebo in M16-063/ABBV-599 in M16-763
Reporting group description:	
Placebo in M16-063; 60 mg elsubrutinib capsule once a day by mouth for 48 weeks and 15 mg film-coated upadacitinib tablet once a day by mouth for 48 weeks in M16-763	

Reporting group values	ABBV-599 in M16-063/ABBV-599 in M16-763	ABBV-105 60 mg/UPA placebo	ABBV-105 20 mg/UPA placebo
Number of subjects	28	16	12
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	57.5	58.6	58.5
standard deviation	± 12.64	± 8.75	± 12.07
Gender categorical			
Units: Subjects			
Female	18	14	12
Male	10	2	0

Reporting group values	ABBV-105 5 mg/UPA placebo	UPA 15 mg/ABBV-105 placebo	Placebo in M16-063/ABBV-599 in M16-763
Number of subjects	12	20	9
Age categorical			
Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	 54.5 ± 12.21	 61.7 ± 8.99	 59.4 ± 9.48
Gender categorical Units: Subjects			
Female	8	18	7
Male	4	2	2

Reporting group values	Total		
Number of subjects	97		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	 -	 	
Gender categorical Units: Subjects			
Female	77		
Male	20		

End points

End points reporting groups

Reporting group title	ABBV-599 in M16-063/ABBV-599 in M16-763
Reporting group description:	
60 mg elsubrutinib capsule once a day by mouth for 48 weeks; 15 mg film-coated upadacitinib tablet once a day by mouth for 48 weeks	
Reporting group title	ABBV-105 60 mg/UPA placebo
Reporting group description:	
60 mg elsubrutinib capsule once a day by mouth for 48 weeks; placebo film-coated tablet for upadacitinib once a day by mouth for 48 weeks	
Reporting group title	ABBV-105 20 mg/UPA placebo
Reporting group description:	
20 mg elsubrutinib capsule once a day by mouth for 48 weeks; placebo film-coated tablet for upadacitinib once a day by mouth for 48 weeks	
Reporting group title	ABBV-105 5 mg/UPA placebo
Reporting group description:	
5 mg elsubrutinib capsule once a day by mouth for 48 weeks; placebo film-coated tablet for upadacitinib once a day by mouth for 48 weeks	
Reporting group title	UPA 15 mg/ABBV-105 placebo
Reporting group description:	
15 mg film-coated upadacitinib tablet once a day by mouth for 48 weeks; placebo capsule for elsubrutinib once a day by mouth for 48 weeks	
Reporting group title	Placebo in M16-063/ABBV-599 in M16-763
Reporting group description:	
Placebo in M16-063; 60 mg elsubrutinib capsule once a day by mouth for 48 weeks and 15 mg film-coated upadacitinib tablet once a day by mouth for 48 weeks in M16-763	

Primary: Number of Participants with Adverse Events (AEs)

End point title	Number of Participants with Adverse Events (AEs)[1]
End point description:	
An adverse event (AE) is defined as any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product which does not necessarily have a causal relationship with this treatment. The investigator assesses the relationship of each event to the use of study drug as either having a reasonable possibility or no reasonable possibility. A serious adverse event (SAE) is an event that results in death, is life-threatening, requires or prolongs hospitalization, results in a congenital anomaly, persistent or significant disability/incapacity or is an important medical event that, based on medical judgment, may jeopardize the participant and may require medical or surgical intervention to prevent any of the outcomes listed above. Treatment-emergent adverse events/treatment-emergent serious adverse events (TEAEs/TESAEs) are defined as any event that began or worsened in severity after the first dose of study drug.	

End point type	Primary
End point timeframe:	
On or after the first dose of study drug in Study M16-763, and up to 30 days after the last dose of study drug in Study M16-763, up to 52 weeks	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive data are summarized for this end point per protocol.

End point values	ABBV-599 in M16-063/ABBV-599 in M16-763	ABBV-105 60 mg/UPA placebo	ABBV-105 20 mg/UPA placebo	ABBV-105 5 mg/UPA placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28[2]	16[3]	12[4]	12[5]
Units: participants	11	10	3	5

Notes:

[2] - Safety Analysis Set: those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763

[3] - Safety Analysis Set: those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763

[4] - Safety Analysis Set: those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763

[5] - Safety Analysis Set: those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763

End point values	UPA 15 mg/ABBV-105 placebo	Placebo in M16-063/ABBV-599 in M16-763		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[6]	9[7]		
Units: participants	7	3		

Notes:

[6] - Safety Analysis Set: those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763

[7] - Safety Analysis Set: those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Disease Activity Score 28 C-reactive protein [DAS28-CRP]) from Baseline of Study M16-063 at each study visit in Study M16-763

End point title	Change in Disease Activity Score 28 C-reactive protein [DAS28-CRP]) from Baseline of Study M16-063 at each study visit in Study M16-763

End point description:

The DAS28-CRP is a composite index used to assess rheumatoid arthritis disease activity, calculated based on the tender joint count (out of 28 evaluated joints), swollen joint count (out of 28 evaluated joints), Patient's Global Assessment of Disease Activity (0-100 mm), and high-sensitivity C-reactive protein (hsCRP; in mg/L). Scores on the DAS28-CRP range from 0 to approximately 10, where higher scores indicate more disease activity. A negative change from Baseline indicates improvement in disease activity.

End point type	Secondary

End point timeframe:

Baseline in Study M16-063, Weeks 18, 24, 30, 36, 48, and 60 in Study M16-763

End point values	ABBV-599 in M16-063/ABBV-599 in M16-763	ABBV-105 60 mg/UPA placebo	ABBV-105 20 mg/UPA placebo	ABBV-105 5 mg/UPA placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26[8]	15[9]	7[10]	10[11]
Units: units on a scale				
arithmetic mean (confidence interval 95%)				
Week 18 (n= 22, 15, 7, 10, 18, 8)	-3.27 (-3.79 to -2.75)	-1.98 (-2.83 to -1.12)	-1.93 (-3.01 to -0.85)	-2.55 (-3.50 to -1.60)
Week 24 (n= 26, 13, 7, 10, 17, 7)	-3.43 (-3.90 to -2.95)	-2.62 (-3.56 to -1.68)	-2.02 (-3.18 to -0.86)	-3.20 (-4.10 to -2.30)
Week 30 (n= 22, 13, 5, 10, 16, 8)	-3.17 (-3.86 to -2.47)	-2.37 (-3.71 to -1.03)	-1.45 (-2.30 to -0.60)	-3.30 (-4.43 to -2.17)
Week 36 (n= 23, 8, 3, 10, 12, 6)	-3.45 (-4.14 to -2.77)	-3.12 (-3.99 to -2.25)	-1.63 (-2.37 to -0.89)	-3.00 (-4.17 to -1.83)
Week 48 (n= 17, 6, 3, 8, 8, 6)	-3.55 (-4.32 to -2.78)	-2.77 (-4.92 to -0.62)	-1.68 (-3.10 to -0.27)	-3.16 (-4.49 to -1.84)
Week 60 (n= 9, 2, 2, 5, 5, 4)	-4.06 (-4.88 to -3.25)	-3.21 (-22.18 to 15.75)	-2.55 (-6.90 to 1.79)	-3.41 (-4.92 to -1.89)

Notes:

[8] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[9] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[10] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[11] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

End point values	UPA 15 mg/ABBV-105 placebo	Placebo in M16-063/ABBV-599 in M16-763		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18[12]	8[13]		
Units: units on a scale				
arithmetic mean (confidence interval 95%)				
Week 18 (n= 22, 15, 7, 10, 18, 8)	-3.88 (-4.63 to -3.14)	-2.87 (-4.05 to -1.68)		
Week 24 (n= 26, 13, 7, 10, 17, 7)	-4.02 (-4.62 to -3.43)	-3.61 (-4.94 to -2.28)		
Week 30 (n= 22, 13, 5, 10, 16, 8)	-3.84 (-4.56 to -3.12)	-4.08 (-4.73 to -3.44)		
Week 36 (n= 23, 8, 3, 10, 12, 6)	-4.15 (-5.02 to -3.29)	-3.77 (-4.79 to -2.75)		
Week 48 (n= 17, 6, 3, 8, 8, 6)	-4.38 (-5.67 to -3.09)	-3.86 (-4.88 to -2.85)		
Week 60 (n= 9, 2, 2, 5, 5, 4)	-4.12 (-5.43 to -2.81)	-3.69 (-5.19 to -2.19)		

Notes:

[12] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[13] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Low Disease Activity (LDA) Based on Disease Activity Score 28 C-reactive Protein (DAS28-CRP)

End point title	Percentage of Participants Achieving Low Disease Activity (LDA) Based on Disease Activity Score 28 C-reactive Protein (DAS28-CRP)

End point description:

The DAS28-CRP is a composite index used to assess rheumatoid arthritis disease activity, calculated based on the tender joint count (out of 28 evaluated joints), swollen joint count (out of 28 evaluated joints), Patient's Global Assessment of Disease Activity (0-100 mm), and high-sensitivity C-reactive protein (hsCRP; in mg/L). Scores on the DAS28-CRP range from 0 to approximately 10, where higher scores indicate more disease activity. Low Disease Activity (LDA) based on DAS28 (CRP) is defined as achieving a DAS28 (CRP) of less than or equal to 3.2.

End point type	Secondary

End point timeframe:

Weeks 18, 24, 30, 36, 48, and 60 in Study M16-763

End point values	ABBV-599 in M16-063/ABBV-599 in M16-763	ABBV-105 60 mg/UPA placebo	ABBV-105 20 mg/UPA placebo	ABBV-105 5 mg/UPA placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27[14]	15[15]	9[16]	10[17]
Units: percentage of participants				
number (confidence interval 95%)				
Week 18 (n= 23, 15, 9, 10, 18, 8)	78.3 (58.10 to 90.34)	26.7 (10.90 to 51.95)	44.4 (18.88 to 73.33)	20.0 (5.67 to 50.98)
Week 24 (n= 27, 13, 9, 10, 17, 7)	77.8 (59.24 to 89.39)	53.8 (29.14 to 76.79)	44.4 (18.88 to 73.33)	50.0 (23.66 to 76.34)
Week 30 (n= 23, 13, 7, 10, 16, 8)	78.3 (58.10 to 90.34)	76.9 (49.74 to 91.82)	28.6 (8.22 to 64.11)	60.0 (31.27 to 83.18)
Week 36 (n= 24, 8, 4, 10, 12, 6)	87.5 (69.00 to 95.66)	87.5 (52.91 to 97.76)	25.0 (4.56 to 69.94)	40.0 (16.82 to 68.73)
Week 48 (n= 18, 6, 4, 8, 8, 6)	77.8 (54.79 to 91.00)	66.7 (30.00 to 90.32)	50.0 (15.00 to 85.00)	37.5 (13.68 to 69.43)
Week 60 (n= 9, 2, 2, 5, 5, 4)	100 (70.09 to 100.00)	50.0 (9.45 to 90.55)	100 (34.24 to 100.00)	60.0 (23.07 to 88.24)

Notes:

[14] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[15] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[16] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[17] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

End point values	UPA 15 mg/ABBV-105 placebo	Placebo in M16-063/ABBV-599 in M16-763		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18[18]	8[19]		
Units: percentage of participants				
number (confidence interval 95%)				

Week 18 (n= 23, 15, 9, 10, 18, 8)	77.8 (54.79 to 91.00)	62.5 (30.57 to 86.32)		
Week 24 (n= 27, 13, 9, 10, 17, 7)	88.2 (65.66 to 96.71)	85.7 (48.69 to 97.43)		
Week 30 (n= 23, 13, 7, 10, 16, 8)	87.5 (63.98 to 96.50)	100 (67.56 to 100.00)		
Week 36 (n= 24, 8, 4, 10, 12, 6)	91.7 (64.61 to 98.51)	100 (60.97 to 100.00)		
Week 48 (n= 18, 6, 4, 8, 8, 6)	87.5 (52.91 to 97.76)	100 (60.97 to 100.00)		
Week 60 (n= 9, 2, 2, 5, 5, 4)	100 (56.55 to 100.00)	75.0 (30.06 to 95.44)		

Notes:

[18] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[19] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Clinical Remission (CR) Based on Disease Activity Score 28 C-reactive Protein (DAS28-CRP)

End point title	Percentage of Participants Achieving Clinical Remission (CR) Based on Disease Activity Score 28 C-reactive Protein (DAS28-CRP)

End point description:

The DAS28-CRP is a composite index used to assess rheumatoid arthritis disease activity, calculated based on the tender joint count (out of 28 evaluated joints), swollen joint count (out of 28 evaluated joints), Patient's Global Assessment of Disease Activity (0-100 mm), and high-sensitivity C-reactive protein (hsCRP; in mg/L). Scores on the DAS28-CRP range from 0 to approximately 10, where higher scores indicate more disease activity. Clinical Remission (CR) based on DAS28 (CRP) is defined as achieving a DAS28 (CRP) of less than 2.6.

End point type	Secondary

End point timeframe:

Weeks 18, 24, 30, 36, 48, and 60 in Study M16-763

End point values	ABBV-599 in M16-063/ABBV-599 in M16-763	ABBV-105 60 mg/UPA placebo	ABBV-105 20 mg/UPA placebo	ABBV-105 5 mg/UPA placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27[20]	15[21]	9[22]	10[23]
Units: percentage of participants				
number (confidence interval 95%)				
Week 18 (n= 23, 15, 9, 10, 18, 8)	56.5 (36.81 to 74.37)	20.0 (7.05 to 45.19)	11.1 (1.99 to 43.50)	20.0 (5.67 to 50.98)
Week 24 (n= 27, 13, 9, 10, 17, 7)	70.4 (51.52 to 84.15)	53.8 (29.14 to 76.79)	33.3 (12.06 to 64.58)	30.0 (10.78 to 60.32)
Week 30 (n= 23, 13, 7, 10, 16, 8)	65.2 (44.89 to 81.19)	46.2 (23.21 to 70.86)	0 (0.00 to 35.43)	40.0 (16.82 to 68.73)
Week 36 (n= 24, 8, 4, 10, 12, 6)	66.7 (46.71 to 82.03)	62.5 (30.57 to 86.32)	0 (0.00 to 48.99)	20.0 (5.67 to 50.98)

Week 48 (n= 18, 6, 4, 8, 8, 6)	72.2 (49.13 to 87.50)	66.7 (30.00 to 90.32)	0 (0.00 to 48.99)	25.0 (7.15 to 59.07)
Week 60 (n= 9, 2, 2, 5, 5, 4)	77.8 (45.26 to 93.68)	50.0 (9.45 to 90.55)	50.0 (9.45 to 90.55)	0 (0.00 to 43.45)

Notes:

[20] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[21] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[22] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[23] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

End point values	UPA 15 mg/ABBV-105 placebo	Placebo in M16-063/ABBV-599 in M16-763		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18[24]	8[25]		
Units: percentage of participants				
number (confidence interval 95%)				
Week 18 (n= 23, 15, 9, 10, 18, 8)	77.8 (54.79 to 91.00)	50.0 (21.52 to 78.48)		
Week 24 (n= 27, 13, 9, 10, 17, 7)	70.6 (46.87 to 86.72)	71.4 (35.89 to 91.78)		
Week 30 (n= 23, 13, 7, 10, 16, 8)	87.5 (63.98 to 96.50)	100 (67.56 to 100.00)		
Week 36 (n= 24, 8, 4, 10, 12, 6)	75.0 (46.77 to 91.11)	66.7 (30.00 to 90.32)		
Week 48 (n= 18, 6, 4, 8, 8, 6)	62.5 (30.57 to 86.32)	83.3 (43.65 to 96.99)		
Week 60 (n= 9, 2, 2, 5, 5, 4)	60.0 (23.07 to 88.24)	75.0 (30.06 to 95.44)		

Notes:

[24] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[25] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Clinical Disease Activity Index (CDAI) From Baseline of Study M16-063

End point title	Change in Clinical Disease Activity Index (CDAI) From Baseline of Study M16-063

End point description:

The CDAI is a composite index for assessing disease activity based on the summation of the total tender joint count (out of 28 evaluated joints), swollen joint count (out of 28 evaluated joints), patient global assessment of disease activity measured on a VAS from 0 to 10 cm, and physician global assessment of disease activity measured on a VAS from 0 to 10 cm. The total CDAI score ranges from 0 to 78 with higher scores indicating higher disease activity. A negative change from Baseline indicates improvement in disease activity.

End point type	Secondary

End point timeframe:

Baseline in Study M16-063, Weeks 18, 24, 30, 36, 48, and 60 in Study M16-763

End point values	ABBV-599 in M16-063/ABBV-599 in M16-763	ABBV-105 60 mg/UPA placebo	ABBV-105 20 mg/UPA placebo	ABBV-105 5 mg/UPA placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26[26]	15[27]	7[28]	9[29]
Units: units on a scale				
arithmetic mean (confidence interval 95%)				
Week 18 (n= 22, 15, 7, 7, 17, 8)	-33.68 (-40.72 to -26.64)	-23.77 (-32.65 to -14.90)	-19.16 (-28.05 to -10.26)	-27.00 (-42.89 to -11.11)
Week 24 (n= 26, 13, 7, 9, 16, 8)	-33.47 (-39.66 to -27.27)	-27.20 (-34.18 to -20.22)	-19.84 (-30.65 to -9.03)	-35.59 (-45.25 to -25.93)
Week 30 (n= 22, 13, 5, 9, 15, 8)	-32.07 (-40.11 to -24.03)	-22.40 (-34.25 to -10.55)	-16.72 (-22.28 to -11.16)	-35.92 (-46.64 to -25.20)
Week 36 (n= 21, 8, 3, 9, 11, 6)	-35.28 (-43.23 to -27.33)	-28.86 (-36.56 to -21.16)	-19.17 (-32.10 to -6.23)	-33.99 (-47.10 to -20.88)
Week 48 (n= 17, 6, 3, 7, 8, 5)	-36.26 (-45.44 to -27.08)	-22.58 (-41.15 to -4.02)	-18.87 (-36.40 to -1.33)	-34.77 (-49.11 to -20.44)
Week 60 (n= 9, 2, 2, 4, 5, 4)	-37.99 (-49.56 to -26.41)	-29.70 (-216.48 to 157.08)	-24.95 (-78.95 to 29.05)	-37.20 (-56.11 to -18.29)

Notes:

[26] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[27] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[28] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[29] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

End point values	UPA 15 mg/ABBV-105 placebo	Placebo in M16-063/ABBV-599 in M16-763		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17[30]	8[31]		
Units: units on a scale				
arithmetic mean (confidence interval 95%)				
Week 18 (n= 22, 15, 7, 7, 17, 8)	-36.01 (-44.11 to -27.91)	-28.65 (-37.00 to -20.30)		
Week 24 (n= 26, 13, 7, 9, 16, 8)	-38.27 (-45.66 to -30.88)	-32.93 (-41.70 to -24.15)		
Week 30 (n= 22, 13, 5, 9, 15, 8)	-36.86 (-46.20 to -27.52)	-34.00 (-44.11 to -27.91)		
Week 36 (n= 21, 8, 3, 9, 11, 6)	-38.27 (-45.66 to -30.88)	-32.92 (-41.43 to -24.40)		
Week 48 (n= 17, 6, 3, 7, 8, 5)	-36.86 (-46.20 to -27.52)	-35.72 (-45.75 to -25.69)		
Week 60 (n= 9, 2, 2, 4, 5, 4)	-42.20 (-52.14 to -32.26)	-34.38 (-46.14 to -22.61)		

Notes:

[30] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[31] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Low Disease Activity (LDA) Based on Clinical Disease Activity Index (CDAI) Criteria

End point title	Percentage of Participants Achieving Low Disease Activity (LDA) Based on Clinical Disease Activity Index (CDAI) Criteria

End point description:

The CDAI is a composite index for assessing disease activity based on the summation of the total tender joint count (out of 28 evaluated joints), swollen joint count (out of 28 evaluated joints), patient global assessment of disease activity measured on a VAS from 0 to 10 cm, and physician global assessment of disease activity measured on a VAS from 0 to 10 cm. The total CDAI score ranges from 0 to 78 with higher scores indicating higher disease activity. Low Disease Activity (LDA) based on CDAI is defined as achieving a total CDAI score of less than or equal to 10.

End point type	Secondary

End point timeframe:

Weeks 18, 24, 30, 36, 48, and 60 in Study M16-763

End point values	ABBV-599 in M16-063/ABBV-599 in M16-763	ABBV-105 60 mg/UPA placebo	ABBV-105 20 mg/UPA placebo	ABBV-105 5 mg/UPA placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27[32]	15[33]	9[34]	10[35]
Units: percentage of participants				
number (confidence interval 95%)				
Week 18 (n= 23, 15, 9, 8, 18, 8)	82.6 (62.86 to 93.02)	40.0 (19.82 to 64.25)	44.4 (18.88 to 73.33)	50.0 (21.52 to 78.48)
Week 24 (n= 27, 13, 9, 10, 17, 8)	88.9 (71.94 to 96.15)	69.2 (42.37 to 87.32)	55.6 (26.67 to 81.12)	80.0 (49.02 to 94.33)
Week 30 (n= 23, 13, 7, 10, 16, 8)	78.3 (58.10 to 90.34)	76.9 (49.74 to 91.82)	42.9 (15.82 to 74.95)	80.0 (49.02 to 94.33)
Week 36 (n= 22, 8, 4, 10, 12, 6)	86.4 (66.67 to 95.25)	87.5 (52.91 to 97.76)	75.0 (30.06 to 95.44)	70.0 (39.68 to 89.22)
Week 48 (n= 18, 6, 4, 8, 8, 5)	77.8 (54.79 to 91.00)	66.7 (30.00 to 90.32)	75.0 (30.06 to 95.44)	62.5 (30.57 to 86.32)
Week 60 (n= 9, 2, 2, 5, 5, 4)	100 (70.09 to 100.00)	50.0 (9.45 to 90.55)	100 (34.24 to 100.00)	80.0 (37.55 to 96.38)

Notes:

[32] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[33] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[34] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[35] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

End point values	UPA 15 mg/ABBV-105 placebo	Placebo in M16-063/ABBV-599 in M16-763		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18[36]	8[37]		
Units: percentage of participants				
number (confidence interval 95%)				
Week 18 (n= 23, 15, 9, 8, 18, 8)	77.8 (54.79 to 91.00)	62.5 (30.57 to 86.32)		
Week 24 (n= 27, 13, 9, 10, 17, 8)	88.2 (65.66 to 96.71)	100 (67.56 to 100.00)		
Week 30 (n= 23, 13, 7, 10, 16, 8)	81.3 (56.99 to 93.41)	100 (67.56 to 100.00)		
Week 36 (n= 22, 8, 4, 10, 12, 6)	83.3 (55.20 to 95.30)	100 (60.97 to 100.00)		
Week 48 (n= 18, 6, 4, 8, 8, 5)	87.5 (52.91 to 97.76)	100 (56.55 to 100.00)		
Week 60 (n= 9, 2, 2, 5, 5, 4)	80.0 (37.55 to 96.38)	75.0 (30.06 to 95.44)		

Notes:

[36] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[37] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Clinical Remission (CR) Based on Clinical Disease Activity Index (CDAI) Criteria

End point title	Percentage of Participants Achieving Clinical Remission (CR) Based on Clinical Disease Activity Index (CDAI) Criteria

End point description:

The CDAI is a composite index for assessing disease activity based on the summation of the total tender joint count (out of 28 evaluated joints), swollen joint count (out of 28 evaluated joints), patient global assessment of disease activity measured on a VAS from 0 to 10 cm, and physician global assessment of disease activity measured on a VAS from 0 to 10 cm. The total CDAI score ranges from 0 to 78 with higher scores indicating higher disease activity. Complete Remission (CR) based on CDAI is defined as achieving a total CDAI score of less than or equal to 2.8.

End point type	Secondary

End point timeframe:

Weeks 18, 24, 30, 36, 48, and 60 in Study M16-763

End point values	ABBV-599 in M16-063/ABBV-599 in M16-763	ABBV-105 60 mg/UPA placebo	ABBV-105 20 mg/UPA placebo	ABBV-105 5 mg/UPA placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27[38]	15[39]	9[40]	10[41]
Units: percentage of participants				
arithmetic mean (confidence interval 95%)				
Week 18 (n= 23, 15, 9, 8, 18, 8)	17.4 (6.98 to 37.14)	13.3 (3.74 to 37.88)	11.1 (1.99 to 43.50)	12.5 (2.24 to 47.09)
Week 24 (n= 27, 13, 9, 10. 17, 8)	29.6 (15.85 to 48.48)	23.1 (8.18 to 50.26)	11.1 (1.99 to 43.50)	10.0 (1.79 to 40.42)
Week 30 (n= 23, 13, 7, 10, 16, 8)	26.1 (12.55 to 46.47)	30.8 (12.68 to 57.63)	14.3 (2.57 to 51.31)	30.0 (10.78 to 60.32)
Week 36 (n= 22, 8, 4, 10, 12, 6)	36.4 (19.73 to 57.05)	25.0 (7.15 to 59.07)	25.0 (4.56 to 69.94)	10.0 (1.79 to 40.42)
Week 48 (n= 18, 6, 4, 8, 8, 5)	44.4 (24.56 to 66.28)	33.3 (9.68 to 70.00)	0 (0.00 to 48.99)	12.5 (2.24 to 47.09)
Week 60 (n= 9, 2, 2, 5, 5, 4)	33.3 (12.06 to 64.58)	50.0 (9.45 to 90.55)	50.0 (9.45 to 90.55)	20.0 (3.62 to 62.45)

Notes:

[38] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[39] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[40] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[41] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

End point values	UPA 15 mg/ABBV-105 placebo	Placebo in M16-063/ABBV-599 in M16-763		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18[42]	8[43]		
Units: percentage of participants				
arithmetic mean (confidence interval 95%)				
Week 18 (n= 23, 15, 9, 8, 18, 8)	55.6 (33.72 to 75.44)	25.0 (7.15 to 59.07)		
Week 24 (n= 27, 13, 9, 10. 17, 8)	58.8 (36.01 to 78.39)	50.0 (21.52 to 78.48)		
Week 30 (n= 23, 13, 7, 10, 16, 8)	43.8 (23.10 to 66.82)	87.5 (52.91 to 97.76)		
Week 36 (n= 22, 8, 4, 10, 12, 6)	41.7 (19.33 to 68.05)	50.0 (18.76 to 81.24)		
Week 48 (n= 18, 6, 4, 8, 8, 5)	50.0 (21.52 to 78.48)	100 (56.55 to 100.00)		
Week 60 (n= 9, 2, 2, 5, 5, 4)	60.0 (23.07 to 88.24)	50.0 (15.00 to 85.00)		

Notes:

[42] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[43] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With an American College of Rheumatology 20% (ACR20) Response

End point title	Percentage of Participants With an American College of Rheumatology 20% (ACR20) Response

End point description:

Participants who met the following 3 conditions for improvement from baseline of Study M16-063 were classified as meeting the American College of Rheumatology 20% response (ACR20) criteria:
1. ≥ 20% improvement in 68-tender joint count from Baseline of Study M16-063
2. ≥ 20% improvement in 66-swollen joint count from Baseline of Study M16-063 and
3. ≥ 20% improvement in at least 3 of the 5 following parameters from Baseline of Study M16-063:
• Patient's Assessment of Pain (Visual Analog Scale [VAS])
• Patient's Global Assessment of Disease Activity (PtGA)
• Physician's Global Assessment of Disease Activity (PhGA)
• Health Assessment Questionnaire Disability Index (HAQ-DI)
• High-sensitivity C-reactive protein (hsCRP)

End point type	Secondary

End point timeframe:

Baseline in Study M16-063, Weeks 18, 24, 30, 36, 48, and 60 in Study M16-763

End point values	ABBV-599 in M16-063/ABBV-599 in M16-763	ABBV-105 60 mg/UPA placebo	ABBV-105 20 mg/UPA placebo	ABBV-105 5 mg/UPA placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26[44]	15[45]	7[46]	10[47]
Units: percentage of participants				
number (confidence interval 95%)				
Week 18 (n=22, 15, 7, 9, 17, 8)	90.9 (72.19 to 97.47)	80.0 (54.81 to 92.95)	57.1 (25.05 to 84.18)	66.7 (35.42 to 87.94)
Week 24 (n= 26, 14, 7, 9, 16, 8)	96.2 (81.11 to 99.32)	92.9 (68.53 to 98.73)	85.7 (48.69 to 97.43)	77.8 (45.26 to 93.68)
Week 30 (n= 22, 13, 6, 10, 16, 8)	86.4 (66.67 to 95.25)	69.2 (42.37 to 87.32)	50.0 (18.76 to 81.24)	80.0 (49.02 to 94.33)
Week 36 (n= 23, 8, 3, 9, 12, 6)	87.0 (67.87 to 95.46)	87.5 (52.91 to 97.76)	66.7 (20.77 to 93.85)	88.9 (56.50 to 98.01)
Week 48 (n= 17, 6, 3, 7, 8, 6)	94.1 (73.02 to 98.95)	83.3 (43.65 to 96.99)	66.7 (20.77 to 93.85)	85.7 (48.69 to 97.43)
Week 60 (n= 9, 2, 2, 4, 5, 4)	88.9 (56.50 to 98.01)	100 (34.24 to 100.00)	100 (34.24 to 100.00)	75.0 (30.06 to 95.44)

Notes:

[44] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data
[45] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data
[46] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data
[47] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

End point values	UPA 15 mg/ABBV-105 placebo	Placebo in M16-063/ABBV-599 in M16-763		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17[48]	8[49]		
Units: percentage of participants				

number (confidence interval 95%)				
Week 18 (n=22, 15, 7, 9, 17, 8)	88.2 (65.66 to 96.71)	75.0 (40.93 to 92.85)		
Week 24 (n= 26, 14, 7, 9, 16, 8)	93.8 (71.67 to 98.89)	100 (67.56 to 100.00)		
Week 30 (n= 22, 13, 6, 10, 16, 8)	87.5 (63.98 to 96.50)	100 (67.56 to 100.00)		
Week 36 (n= 23, 8, 3, 9, 12, 6)	91.7 (64.61 to 98.51)	83.3 (43.65 to 96.99)		
Week 48 (n= 17, 6, 3, 7, 8, 6)	87.5 (52.91 to 97.76)	100 (60.97 to 100.00)		
Week 60 (n= 9, 2, 2, 4, 5, 4)	100 (56.55 to 100.00)	100 (51.01 to 100.00)		

Notes:

[48] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[49] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With an American College of Rheumatology 50% (ACR50) Response

End point title	Percentage of Participants With an American College of Rheumatology 50% (ACR50) Response

End point description:

Participants who met the following 3 conditions for improvement from baseline of Study M16-063 were classified as
meeting the American College of Rheumatology 50% response (ACR50) criteria:
1. ≥ 50% improvement in 68-tender joint count from Baseline of Study M16-063
2. ≥ 50% improvement in 66-swollen joint count from Baseline of Study M16-063 and
3. ≥ 50% improvement in at least 3 of the 5 following parameters from Baseline of Study M16-063:
- Patient's Assessment of Pain (Visual Analog Scale [VAS])
- Patient’s Global Assessment of Disease Activity (PtGA)
- Physician’s Global Assessment of Disease Activity (PhGA)
- Health Assessment Questionnaire Disability Index (HAQ-DI)
- High-sensitivity C-reactive protein (hsCRP)

End point type	Secondary

End point timeframe:

Baseline in Study M16-063, Weeks 18, 24, 30, 36, 48, and 60 in Study M16-763

End point values	ABBV-599 in M16-063/ABBV-599 in M16-763	ABBV-105 60 mg/UPA placebo	ABBV-105 20 mg/UPA placebo	ABBV-105 5 mg/UPA placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26[50]	15[51]	10[52]	10[53]
Units: percentage of participants				
number (confidence interval 95%)				
Week 18 (n= 22, 15, 10, 10, 17, 8)	68.2 (47.32 to 83.64)	46.7 (24.81 to 69.88)	40.0 (16.82 to 68.73)	40.0 (16.82 to 68.73)
Week 24 (n= 26, 14, 7, 9, 16, 8)	76.9 (57.95 to 88.97)	64.3 (38.76 to 83.66)	42.9 (15.82 to 74.95)	66.7 (35.42 to 87.94)

Week 30 (n= 22, 13, 6, 10, 16, 8)	63.6 (42.95 to 80.27)	61.5 (35.52 to 82.29)	16.7 (3.01 to 56.35)	60.0 (31.27 to 83.18)
Week 36 (n= 23, 8, 3, 9, 12, 6)	82.6 (62.86 to 93.02)	62.5 (30.57 to 86.32)	33.3 (6.15 to 79.23)	66.7 (35.42 to 87.94)
Week 48 (n= 17, 6, 3, 7, 8, 6)	82.4 (58.97 to 93.81)	66.7 (30.00 to 90.32)	66.7 (20.77 to 93.85)	71.4 (35.89 to 91.78)
Week 60 (n= 9, 2, 2, 4, 5, 4)	88.9 (56.50 to 98.01)	50.0 (9.45 to 90.55)	100 (34.24 to 100.00)	75.0 (30.06 to 95.44)

Notes:

[50] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data
[51] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data
[52] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data
[53] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

End point values	UPA 15 mg/ABBV-105 placebo	Placebo in M16-063/ABBV-599 in M16-763		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17[54]	8[55]		
Units: percentage of participants				
number (confidence interval 95%)				
Week 18 (n= 22, 15, 10, 10, 17, 8)	70.6 (46.87 to 86.72)	62.5 (30.57 to 86.32)		
Week 24 (n= 26, 14, 7, 9, 16, 8)	87.5 (63.98 to 96.50)	100 (67.56 to 100.00)		
Week 30 (n= 22, 13, 6, 10, 16, 8)	87.5 (63.98 to 96.50)	100 (67.56 to 100.00)		
Week 36 (n= 23, 8, 3, 9, 12, 6)	75.0 (46.77 to 91.11)	66.7 (30.00 to 90.32)		
Week 48 (n= 17, 6, 3, 7, 8, 6)	87.5 (52.91 to 97.76)	83.3 (43.65 to 96.99)		
Week 60 (n= 9, 2, 2, 4, 5, 4)	100 (56.55 to 100.00)	100 (51.01 to 100.00)		

Notes:

[54] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data
[55] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With an American College of Rheumatology 70% (ACR70) Response

End point title	Percentage of Participants With an American College of Rheumatology 70% (ACR70) Response

End point description:

Participants who met the following 3 conditions for improvement from baseline of Study M16-063 were classified as meeting the American College of Rheumatology 70% response (ACR70) criteria:
1. ≥ 70% improvement in 68-tender joint count from Baseline of Study M16-063
2. ≥ 70% improvement in 66-swollen joint count from Baseline of Study M16-063 and
3. ≥ 70% improvement in at least 3 of the 5 following parameters from Baseline of Study M16-063:
• Patient's Assessment of Pain (Visual Analog Scale [VAS])
• Patient’s Global Assessment of Disease Activity (PtGA)
• Physician’s Global Assessment of Disease Activity (PhGA)
• Health Assessment Questionnaire Disability Index (HAQ-DI)

• High-sensitivity C-reactive protein (hsCRP)

End point type	Secondary

End point timeframe:

Baseline in Study M16-063, Weeks 18, 24, 30, 36, 48, and 60 in Study M16-763

End point values	ABBV-599 in M16-063/ABBV-599 in M16-763	ABBV-105 60 mg/UPA placebo	ABBV-105 20 mg/UPA placebo	ABBV-105 5 mg/UPA placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26[56]	15[57]	10[58]	12[59]
Units: percentage of participants				
number (confidence interval 95%)				
Week 18 (n= 23, 15, 10, 12, 18, 8)	47.8 (29.24 to 67.04)	33.3 (15.18 to 58.29)	20.0 (5.67 to 50.98)	25.0 (8.89 to 53.23)
Week 24 (n= 26, 14, 8, 9, 16, 8)	57.7 (38.95 to 74.46)	42.9 (21.38 to 67.41)	12.5 (2.24 to 47.09)	55.6 (26.67 to 81.12)
Week 30 (n= 22, 13, 7, 10, 16, 8)	63.6 (42.95 to 80.27)	46.2 (23.21 to 70.86)	14.3 (2.57 to 51.31)	60.0 (31.27 to 83.18)
Week 36 (n= 23, 8, 4, 9, 12, 6)	78.3 (58.10 to 90.34)	50.0 (21.52 to 78.48)	25.0 (4.56 to 69.94)	44.4 (18.88 to 73.33)
Week 48 (n= 17, 6, 4, 7, 8, 6)	58.8 (36.01 to 78.39)	50.0 (18.76 to 81.24)	25.0 (4.56 to 69.94)	42.9 (15.82 to 74.95)
Week 60 (n= 9, 2, 2, 4, 5, 4)	88.9 (56.50 to 98.01)	50.0 (9.45 to 90.55)	50.0 (9.45 to 90.55)	25.0 (4.56 to 69.94)

Notes:

[56] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[57] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[58] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[59] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

End point values	UPA 15 mg/ABBV-105 placebo	Placebo in M16-063/ABBV-599 in M16-763		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18[60]	8[61]		
Units: percentage of participants				
number (confidence interval 95%)				
Week 18 (n= 23, 15, 10, 12, 18, 8)	55.6 (33.72 to 75.44)	37.5 (13.68 to 69.43)		
Week 24 (n= 26, 14, 8, 9, 16, 8)	62.5 (38.64 to 81.52)	87.5 (52.91 to 97.76)		
Week 30 (n= 22, 13, 7, 10, 16, 8)	68.8 (44.40 to 85.84)	87.5 (52.91 to 97.76)		
Week 36 (n= 23, 8, 4, 9, 12, 6)	75.0 (46.77 to 91.11)	66.7 (30.00 to 90.32)		
Week 48 (n= 17, 6, 4, 7, 8, 6)	75.0 (40.93 to 92.85)	83.3 (43.65 to 96.99)		
Week 60 (n= 9, 2, 2, 4, 5, 4)	60.0 (23.07 to 88.24)	75.0 (30.06 to 95.44)		

Notes:

[60] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data
[61] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Swollen Joint Count 66 (SJC66) From Baseline of Study M16-063

End point title	Change in Swollen Joint Count 66 (SJC66) From Baseline of Study M16-063

End point description:

Sixty-six joints were assessed for swelling by physical examination. Swelling of each joint was classified as present (1) or absent (0), for a total
possible score of 0 (0 joints with swelling) to 66 (worst possible score/66 joints with swelling). Negative values indicate improvement from baseline.

End point type	Secondary

End point timeframe:

Baseline in Study M16-063, Weeks 18, 24, 30, 36, 48, and 60 in Study M16-763

End point values	ABBV-599 in M16-063/ABBV-599 in M16-763	ABBV-105 60 mg/UPA placebo	ABBV-105 20 mg/UPA placebo	ABBV-105 5 mg/UPA placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28[62]	16[63]	11[64]	12[65]
Units: swollen joint counts				
arithmetic mean (confidence interval 95%)				
Week 18 (n= 28, 16, 11, 12, 20, 9)	-11.50 (-13.66 to -9.34)	-9.88 (-14.37 to -5.38)	-8.00 (-11.28 to -4.72)	-13.42 (-18.40 to -8.43)
Week 24 (n= 27, 13, 9, 10, 17, 8)	-11.37 (-13.85 to -9.49)	-10.54 (-14.25 to -6.82)	-7.67 (-10.13 to -5.21)	-15.60 (-21.14 to -10.06)
Week 30 (n= 23, 13, 7, 10, 16, 8)	-11.87 (-14.53 to -9.21)	-7.69 (-11.64 to -3.74)	-5.86 (-8.27 to -3.44)	-15.50 (-21.05 to -9.95)
Week 36 (n= 24, 8, 4, 10, 12, 6)	-12.38 (-14.84 to -9.91)	-10.13 (-13.42 to -6.83)	-7.75 (-11.73 to -3.77)	-14.60 (-21.38 to -7.82)
Week 48 (n= 18, 6, 4, 8, 8, 6)	-13.67 (-16.57 to -10.77)	-8.00 (-16.13 to 0.13)	-8.00 (-11.90 to -4.10)	-15.88 (-21.34 to -10.41)
Week 60 (n= 9, 2, 2, 5, 5, 4)	-14.44 (-17.73 to -11.16)	-12.50 (-18.85 to -6.15)	-7.50 (-39.27 to 24.27)	-15.40 (-23.66 to -7.14)

Notes:

[62] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data
[63] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data
[64] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data
[65] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/

available data

End point values	UPA 15 mg/ABBV-105 placebo	Placebo in M16-063/ABBV-599 in M16-763		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[66]	9[67]		
Units: swollen joint counts				
arithmetic mean (confidence interval 95%)				
Week 18 (n= 28, 16, 11, 12, 20, 9)	-12.80 (-16.11 to -9.49)	-9.78 (-13.06 to -6.50)		
Week 24 (n= 27, 13, 9, 10, 17, 8)	-13.24 (-16.48 to -9.99)	-10.38 (-14.22 to -6.53)		
Week 30 (n= 23, 13, 7, 10, 16, 8)	-13.44 (-17.11 to -9.77)	-10.75 (-14.61 to -6.89)		
Week 36 (n= 24, 8, 4, 10, 12, 6)	-14.25 (-18.71 to -9.79)	-10.50 (-14.79 to -6.21)		
Week 48 (n= 18, 6, 4, 8, 8, 6)	-15.75 (-21.84 to -9.66)	-10.67 (-15.34 to -5.99)		
Week 60 (n= 9, 2, 2, 5, 5, 4)	-13.00 (-20.80 to -5.20)	-11.25 (-16.00 to -6.50)		

Notes:

[66] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[67] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Tender Joint Count 68 (TJC68) From Baseline of Study M16-063

End point title	Change in Tender Joint Count 68 (TJC68) From Baseline of Study M16-063

End point description:

Sixty-eight joints were assessed for tenderness by physical examination. Pain or tenderness of each joint was classified as present (1) or absent (0), for a total possible score of 0 (0 joints with tenderness) to 68 (worst possible score/68 joints with tenderness). Negative values indicate improvement from baseline.

End point type	Secondary

End point timeframe:

Baseline in Study M16-063, Weeks 18, 24, 30, 36, 48, and 60 in Study M16-763

End point values	ABBV-599 in M16-063/ABBV-599 in M16-763	ABBV-105 60 mg/UPA placebo	ABBV-105 20 mg/UPA placebo	ABBV-105 5 mg/UPA placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28[68]	16[69]	11[70]	12[71]
Units: tender joint counts				
arithmetic mean (confidence interval 95%)				
Week 18 (n= 28, 16, 11, 12, 20, 9)	-17.29 (-20.95 to -13.62)	-12.69 (-18.77 to -6.61)	-9.82 (-13.63 to -6.01)	-14.17 (-21.70 to -6.63)
Week 24 (n= 27, 13, 9, 10, 17, 8)	-17.93 (-21.84 to -14.02)	-15.77 (-19.37 to -12.17)	-8.11 (-10.95 to -5.28)	-20.20 (-26.97 to -13.43)
Week 30 (n= 23, 13, 7, 10, 16, 8)	-16.30 (-20.32 to -12.29)	-9.54 (-18.16 to -0.92)	-4.57 (-7.29 to -1.86)	-19.80 (-27.25 to -12.35)
Week 36 (n= 24, 8, 4, 10, 12, 6)	-16.42 (-20.15 to -12.68)	-15.25 (-19.85 to -10.65)	-8.00 (-15.46 to -0.54)	-18.40 (-26.99 to -9.81)
Week 48 (n= 18, 6, 4, 8, 8, 6)	-17.33 (-21.05 to -13.61)	-12.33 (-23.09 to -1.58)	-5.50 (-14.64 to 3.64)	-18.88 (-28.63 to -9.12)
Week 60 (n= 9, 2, 2, 5, 5, 4)	-19.78 (-25.14 to -14.41)	-19.00 (-82.53 to 44.53)	-11.50 (-81.38 to 58.38)	-20.20 (-35.42 to -4.98)

Notes:

[68] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[69] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[70] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[71] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

End point values	UPA 15 mg/ABBV-105 placebo	Placebo in M16-063/ABBV-599 in M16-763		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[72]	9[73]		
Units: tender joint counts				
arithmetic mean (confidence interval 95%)				
Week 18 (n= 28, 16, 11, 12, 20, 9)	-19.75 (-25.63 to -13.87)	-10.67 (-16.21 to -5.12)		
Week 24 (n= 27, 13, 9, 10, 17, 8)	-20.76 (-27.39 to -14.14)	-14.25 (-18.44 to -10.06)		
Week 30 (n= 23, 13, 7, 10, 16, 8)	-20.50 (-28.45 to -12.55)	-14.88 (-18.60 to -11.15)		
Week 36 (n= 24, 8, 4, 10, 12, 6)	-24.92 (-33.96 to -15.88)	-14.83 (-19.21 to -10.46)		
Week 48 (n= 18, 6, 4, 8, 8, 6)	-28.88 (-41.80 to -15.95)	-15.00 (-20.10 to -9.90)		
Week 60 (n= 9, 2, 2, 5, 5, 4)	-26.20 (-36.90 to -15.50)	-15.50 (-21.52 to -9.48)		

Notes:

[72] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[73] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Participant's Assessment of Pain (Visual Analog Scale [VAS]) From Baseline of Study M16-063

End point title	Change in Participant's Assessment of Pain (Visual Analog Scale [VAS]) From Baseline of Study M16-063

End point description:

Participants rated their pain on a visual analogue scale (VAS) of 0 to 100 (mm), with 0 representing no pain and 100 representing the worst possible pain. Negative values indicate improvement from baseline.

End point type	Secondary

End point timeframe:

Baseline in Study M16-063, Weeks 18, 24, 30, 36, 48, and 60 in Study M16-763

End point values	ABBV-599 in M16-063/ABBV-599 in M16-763	ABBV-105 60 mg/UPA placebo	ABBV-105 20 mg/UPA placebo	ABBV-105 5 mg/UPA placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26[74]	15[75]	7[76]	10[77]
Units: units on a scale				
arithmetic mean (confidence interval 95%)				
Week 18 (n= 22, 15, 7, 10, 18, 8)	-49.68 (-62.42 to -36.94)	-34.67 (-51.73 to -17.61)	-25.57 (-56.51 to 5.37)	-32.50 (-53.25 to -11.75)
Week 24 (n= 26, 14, 7, 10, 17, 8)	-45.46 (-58.31 to -32.61)	-48.36 (-60.60 to -36.11)	-29.43 (-50.47 to -8.39)	-42.00 (-61.74 to -22.26)
Week 30 (n= 22, 13, 5, 10, 16, 8)	-48.18 (-61.90 to -34.46)	-40.62 (-63.40 to -17.83)	-20.00 (-48.48 to 8.48)	-45.90 (-70.64 to -21.16)
Week 36 (n= 23, 8, 3, 10, 12, 6)	-49.22 (-61.84 to -36.59)	-47.13 (-72.05 to -22.20)	-25.67 (-120.27 to 68.94)	-46.70 (-63.40 to -30.00)
Week 48 (n= 17, 6, 3, 8, 8, 6)	-60.06 (-72.78 to -47.34)	-49.00 (-72.85 to -25.15)	-35.00 (-69.15 to -0.85)	-56.13 (-82.80 to -29.45)
Week 60 (n= 9, 2, 2, 5, 5, 4)	-54.67 (-77.99 to -31.34)	-52.00 (-522.13 to 418.13)	-45.50 (-140.80 to 49.80)	-58.80 (-73.74 to -43.86)

Notes:

[74] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[75] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[76] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[77] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

End point values	UPA 15 mg/ABBV-105 placebo	Placebo in M16-063/ABBV-599 in M16-763		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18[78]	8[79]		
Units: units on a scale				
arithmetic mean (confidence interval 95%)				
Week 18 (n= 22, 15, 7, 10, 18, 8)	-56.17 (-72.40 to -39.93)	-47.88 (-76.92 to -18.83)		

Week 24 (n= 26, 14, 7, 10, 17, 8)	-57.76 (-73.67 to -41.86)	-59.38 (-80.35 to -38.40)		
Week 30 (n= 22, 13, 5, 10, 16, 8)	-53.63 (-71.19 to -36.06)	-60.25 (-80.74 to -39.76)		
Week 36 (n= 23, 8, 3, 10, 12, 6)	-58.83 (-80.69 to -36.98)	-54.83 (-90.68 to -18.98)		
Week 48 (n= 17, 6, 3, 8, 8, 6)	-58.75 (-82.80 to -34.70)	-61.50 (-94.46 to -28.54)		
Week 60 (n= 9, 2, 2, 5, 5, 4)	-61.00 (-88.13 to -33.87)	-55.00 (-100.36 to -9.64)		

Notes:

[78] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[79] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Patient's Global Assessment of Disease Activity (PtGA) From Baseline of Study M16-063

End point title	Change in Patient's Global Assessment of Disease Activity (PtGA) From Baseline of Study M16-063

End point description:

Participants rated their disease activity for the past 24 hours using a Patient's Global Assessment of Disease Activity Global visual analogue scale (VAS). The range is 0 to 100 mm, with 0 representing no disease activity and 100 representing severe disease activity. Negative values indicate improvement from baseline.

End point type	Secondary

End point timeframe:

Baseline in Study M16-063, Weeks 18, 24, 30, 36, 48, and 60 in Study M16-763

End point values	ABBV-599 in M16-063/ABBV-599 in M16-763	ABBV-105 60 mg/UPA placebo	ABBV-105 20 mg/UPA placebo	ABBV-105 5 mg/UPA placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26[80]	15[81]	7[82]	10[83]
Units: units on a scale				
arithmetic mean (confidence interval 95%)				
Week 18 (n= 22, 15, 7, 10. 18, 8)	-45.18 (-58.36 to -32.00)	-34.07 (-50.11 to -18.03)	-28.57 (-61.69 to 4.55)	-35.70 (-56.96 to -14.44)
Week 24 (n= 26, 14, 7, 10, 17, 8)	-48.62 (-59.37 to -37.87)	-45.93 (-60.14 to -31.72)	-33.29 (-59.62 to -6.95)	-45.20 (-61.30 to -29.10)
Week 30 (n= 22, 13, 5, 10, 16, 8)	-46.18 (-60.77 to -31.60)	-39.69 (-61.63 to -17.76)	-21.40 (-57.54 to 14.74)	-45.20 (-67.27 to -23.13)
Week 36 (n= 23, 8, 3, 10, 12, 6)	-51.70 (-64.00 to -39.39)	-48.63 (-73.95 to -23.30)	-31.67 (-141.65 to 78.32)	-46.20 (-64.52 to -27.88)
Week 48 (n= 17, 6, 3, 8, 8, 6)	-54.24 (-69.66 to -38.81)	-44.00 (-71.07 to -16.93)	-38.67 (-88.62 to 11.28)	-53.13 (-76.82 to -29.43)

Week 60 (n= 9, 2, 2, 5, 5, 4)	-56.67 (-83.18 to -30.16)	-56.00 (-462.60 to 350.60)	-54.50 (-226.03 to 117.03)	-54.60 (-70.61 to -38.59)

Notes:

[80] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[81] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[82] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[83] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

End point values	UPA 15 mg/ABBV-105 placebo	Placebo in M16-063/ABBV-599 in M16-763		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18[84]	8[85]		
Units: units on a scale				
arithmetic mean (confidence interval 95%)				
Week 18 (n= 22, 15, 7, 10. 18, 8)	-56.56 (-72.18 to -40.93)	-40.13 (-67.21 to -13.04)		
Week 24 (n= 26, 14, 7, 10, 17, 8)	-62.47 (-76.09 to -48.85)	-58.13 (-74.96 to -41.29)		
Week 30 (n= 22, 13, 5, 10, 16, 8)	-56.31 (-71.70 to -40.92)	-57.75 (-75.80 to -39.70)		
Week 36 (n= 23, 8, 3, 10, 12, 6)	-61.00 (-81.17 to -40.83)	-53.33 (-84.24 to -22.42)		
Week 48 (n= 17, 6, 3, 8, 8, 6)	-60.75 (-84.13 to -37.37)	-56.67 (-84.14 to -29.19)		
Week 60 (n= 9, 2, 2, 5, 5, 4)	-59.80 (-96.50 to -23.10)	-57.00 (-87.75 to -26.25)		

Notes:

[84] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[85] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Physician's Global Assessment of Disease Activity (PhGA) From Baseline of Study M16-063

End point title	Change in Physician's Global Assessment of Disease Activity (PhGA) From Baseline of Study M16-063

End point description:

The physician assessed a participant’s disease activity at the time of the visit using a Physician's Global Assessment of Disease visual analogue scale (VAS). The range is 0 to 100 mm, with 0 representing no disease activity and 100 representing severe disease activity. Negative values indicate improvement from baseline.

End point type	Secondary

End point timeframe:

Baseline in Study M16-063, Weeks 18, 24, 30, 36, 48, and 60 in Study M16-763

End point values	ABBV-599 in M16-063/ABBV-599 in M16-763	ABBV-105 60 mg/UPA placebo	ABBV-105 20 mg/UPA placebo	ABBV-105 5 mg/UPA placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27[86]	15[87]	7[88]	9[89]
Units: units on a scale				
arithmetic mean (confidence interval 95%)				
Week 18 (n= 23, 15, 7, 7, 17, 8)	-57.22 (-65.56 to -48.87)	-41.00 (-53.42 to -28.58)	-33.00 (-61.23 to -4.77)	-35.00 (-59.98 to -10.02)
Week 24 (n= 27, 14, 7, 9, 16, 8)	-57.93 (-65.61 to -50.25)	-48.36 (-60.05 to -36.66)	-39.43 (-70.88 to -7.98)	-50.89 (-68.36 to -33.42)
Week 30 (n= 23, 13, 5, 9, 15, 8)	-55.04 (-64.27 to -45.82)	-41.23 (-57.85 to -24.61)	-41.80 (-60.33 to -23.27)	-54.78 (-71.11 to -38.45)
Week 36 (n= 22, 8, 3, 9, 11, 6)	-57.55 (-66.96 to -48.13)	-53.75 (-70.49 to -37.01)	-60.00 (-112.58 to -7.42)	-54.78 (-73.97 to -35.58)
Week 48 (n= 18, 6, 3, 7, 8, 5)	-56.39 (-71.53 to -41.24)	-36.83 (-75.18 to 1.52)	-56.67 (-93.29 to -20.04)	-57.14 (-80.22 to -34.07)
Week 60 (n= 9, 2, 2, 4, 5, 4)	-64.33 (-79.18 to -49.48)	-56.00 (-437.19 to 325.19)	-65.00 (-141.24 to 11.24)	-61.50 (-88.83 to -34.17)

Notes:

[86] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[87] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[88] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[89] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

End point values	UPA 15 mg/ABBV-105 placebo	Placebo in M16-063/ABBV-599 in M16-763		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17[90]	8[91]		
Units: units on a scale				
arithmetic mean (confidence interval 95%)				
Week 18 (n= 23, 15, 7, 7, 17, 8)	-59.06 (-69.39 to -48.72)	-55.13 (-82.03 to -28.22)		
Week 24 (n= 27, 14, 7, 9, 16, 8)	-61.19 (-71.90 to -50.47)	-62.38 (-77.73 to -47.02)		
Week 30 (n= 23, 13, 5, 9, 15, 8)	-56.20 (-73.22 to -39.18)	-63.50 (-79.15 to -47.85)		
Week 36 (n= 22, 8, 3, 9, 11, 6)	-68.45 (-81.66 to -55.25)	-65.83 (-89.60 to -42.06)		
Week 48 (n= 18, 6, 3, 7, 8, 5)	-66.13 (-82.33 to -49.92)	-66.40 (-89.67 to -43.13)		
Week 60 (n= 9, 2, 2, 4, 5, 4)	-60.00 (-88.34 to -31.66)	-56.75 (-87.94 to -25.56)		

Notes:

[90] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data
[91] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Health Assessment Questionnaire Disability Index (HAQ-DI) From Baseline of Study M16-063

End point title	Change in Health Assessment Questionnaire Disability Index (HAQ-DI) From Baseline of Study M16-063

End point description:

The Health Assessment Questionnaire - Disability Index is a patient-reported questionnaire that measures the degree of difficulty a person has in accomplishing tasks in 8 functional areas (dressing, arising, eating, walking, hygiene, reaching, gripping, and errands and chores) over the past week. Participants assessed their ability to do each task on a scale from 0 (without any difficulty) to 3 (unable to do). Scores were averaged to provide an overall score ranging from 0 to 3, where 0 represents no disability and 3 represents very severe, high-dependency disability. A negative change from baseline in the overall score indicates improvement.

End point type	Secondary

End point timeframe:

Baseline in Study M16-063, Weeks 18, 24, 30, 36, 48, and 60 in Study M16-763

End point values	ABBV-599 in M16-063/ABBV-599 in M16-763	ABBV-105 60 mg/UPA placebo	ABBV-105 20 mg/UPA placebo	ABBV-105 5 mg/UPA placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25[92]	15[93]	7[94]	10[95]
Units: units on a scale				
arithmetic mean (confidence interval 95%)				
Week 18 (n= 22, 15, 7, 10, 17, 8)	-0.57 (-0.84 to -0.29)	-0.49 (-0.84 to -0.14)	-0.61 (-1.27 to 0.06)	-0.61 (-1.04 to -0.19)
Week 24 (n= 25, 14, 7, 10, 16, 8)	-0.59 (-0.81 to -0.36)	-0.46 (-0.80 to -0.12)	-0.57 (-1.24 to 0.09)	-0.54 (-0.98 to -0.09)
Week 30 (n= 22, 13, 5, 10, 15, 8)	-0.64 (-0.91 to -0.36)	-0.45 (-0.93 to 0.03)	-0.15 (-0.45 to 0.15)	-0.51 (-0.94 to -0.09)
Week 36 (n= 23, 8, 3, 10, 11, 6)	-0.67 (-0.95 to -0.38)	-0.70 (-1.45 to 0.05)	-0.33 (-0.81 to 0.14)	-0.30 (-0.70 to 0.10)
Week 48 (n= 17, 6, 3, 8, 8, 6)	-0.70 (-1.06 to -0.34)	-0.63 (-1.76 to 0.51)	-0.29 (-0.65 to 0.07)	-0.42 (-0.90 to 0.06)
Week 60 (n= 9, 2, 2, 5, 5, 4)	-0.78 (-1.22 to -0.34)	-0.75 (-13.46 to 11.96)	-0.31 (-4.28 to 3.66)	-0.58 (-1.30 to 0.15)

Notes:

[92] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data
[93] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[94] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data
[95] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

End point values	UPA 15 mg/ABBV-105 placebo	Placebo in M16-063/ABBV-599 in M16-763		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17[96]	8[97]		
Units: units on a scale				
arithmetic mean (confidence interval 95%)				
Week 18 (n= 22, 15, 7, 10, 17, 8)	-0.85 (-1.21 to -0.50)	-0.47 (-0.77 to -0.17)		
Week 24 (n= 25, 14, 7, 10, 16, 8)	-0.59 (-0.94 to -0.25)	-0.78 (-1.29 to -0.27)		
Week 30 (n= 22, 13, 5, 10, 15, 8)	-0.73 (-1.10 to -0.35)	-0.75 (-1.17 to -0.33)		
Week 36 (n= 23, 8, 3, 10, 11, 6)	-0.51 (-0.94 to -0.09)	-0.56 (-1.05 to -0.07)		
Week 48 (n= 17, 6, 3, 8, 8, 6)	-0.39 (-0.83 to 0.05)	-0.71 (-1.17 to -0.25)		
Week 60 (n= 9, 2, 2, 5, 5, 4)	-0.48 (-1.77 to 0.82)	-0.72 (-1.61 to 0.18)		

Notes:
[96] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data
[97] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change in High-Sensitivity C-Reactive Protein (Hs-CRP) From Baseline of Study M16-063

End point title	Change in High-Sensitivity C-Reactive Protein (Hs-CRP) From Baseline of Study M16-063

End point description:

C-reactive protein is a blood test marker for inflammation in the body, and levels rise in response to inflammation. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline in Study M16-063, Weeks 18, 24, 30, 36, 48, and 60 in Study M16-763

End point values	ABBV-599 in M16-063/ABBV-599 in M16-763	ABBV-105 60 mg/UPA placebo	ABBV-105 20 mg/UPA placebo	ABBV-105 5 mg/UPA placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28[98]	16[99]	11[100]	12[101]
Units: mg/L				
arithmetic mean (confidence interval				

95%)				
Week 18 (n= 28, 16, 11, 12, 20, 9)	-16.04 (-24.13 to -7.95)	5.34 (-9.84 to 20.53)	-0.96 (-6.20 to 4.28)	-14.85 (-34.27 to 4.57)
Week 24 (n= 27, 14, 9, 10, 17, 7)	-15.08 (-23.26 to -6.90)	-0.20 (-15.16 to 14.76)	-2.18 (-4.30 to -0.06)	-15.09 (-38.53 to 8.34)
Week 30 (n= 23, 13, 7, 10, 16, 8)	-16.61 (-27.35 to -5.88)	-6.00 (-24.37 to 12.36)	-1.66 (-4.91 to 1.59)	-17.11 (-44.18 to 9.95)
Week 36 (n= 24, 8, 4, 10, 12, 6)	-13.88 (-23.43 to -4.32)	-12.43 (-27.58 to 2.73)	-1.58 (-11.33 to 8.18)	-13.61 (-34.50 to 7.28)
Week 48 (n= 18, 6, 4, 8, 8, 6)	-16.41 (-28.14 to -4.69)	-18.38 (-50.37 to 13.60)	-5.99 (-17.43 to 5.45)	-20.18 (-49.36 to 9.00)
Week 60 (n= 9, 2, 2, 5, 5, 4)	-25.69 (-45.41 to -5.98)	-31.46 (-288.63 to 225.71)	-3.98 (-116.05 to 108.09)	-25.58 (-67.98 to 16.83)

Notes:

[98] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[99] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[100] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[101] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

End point values	UPA 15 mg/ABBV-105 placebo	Placebo in M16-063/ABBV-599 in M16-763		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[102]	9[103]		
Units: mg/L				
arithmetic mean (confidence interval 95%)				
Week 18 (n= 28, 16, 11, 12, 20, 9)	-11.48 (-16.88 to -6.07)	-10.00 (-28.36 to 8.35)		
Week 24 (n= 27, 14, 9, 10, 17, 7)	-9.48 (-15.35 to -3.60)	-13.16 (-32.31 to 5.99)		
Week 30 (n= 23, 13, 7, 10, 16, 8)	-9.55 (-14.24 to -4.85)	-16.22 (-28.83 to -3.61)		
Week 36 (n= 24, 8, 4, 10, 12, 6)	-7.76 (-13.95 to -1.56)	-18.34 (-37.30 to 0.62)		
Week 48 (n= 18, 6, 4, 8, 8, 6)	-7.22 (-14.57 to 0.14)	-18.30 (-36.16 to -0.44)		
Week 60 (n= 9, 2, 2, 5, 5, 4)	-3.34 (-23.18 to 16.50)	-12.47 (-33.61 to 8.67)		

Notes:

[102] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[103] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Morning Stiffness Severity From Baseline of Study M16-063

End point title	Change in Morning Stiffness Severity From Baseline of Study M16-063

End point description:

Morning stiffness severity was assessed by a numeric rating-scale (NRS). Participants rated the severity of morning stiffness during the past week from 0 to 10 with 0 representing "not severe" and 10 "very

severe". Negative values indicate improvement from baseline.

Values of -999 and 999 in the table below indicate that the 95% confidence interval is not calculable/estimable because the standard deviation = 0.

End point type	Secondary

End point timeframe:

Baseline in Study M16-063, Weeks 18, 24, 30, 36, 48, and 60 in Study M16-763

End point values	ABBV-599 in M16-063/ABBV-599 in M16-763	ABBV-105 60 mg/UPA placebo	ABBV-105 20 mg/UPA placebo	ABBV-105 5 mg/UPA placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25[104]	15[105]	7[106]	10[107]
Units: units on a scale				
arithmetic mean (confidence interval 95%)				
Week 18 (n= 22, 15, 7, 10, 17, 8)	-4.27 (-5.56 to -2.99)	-2.27 (-3.69 to -0.84)	-2.14 (-4.99 to 0.70)	-3.40 (-6.02 to -0.78)
Week 24 (n= 25, 14, 7, 10, 16, 8)	-4.48 (-5.52 to -3.44)	-2.64 (-3.81 to -1.47)	-3.29 (-5.89 to -0.69)	-3.70 (-5.21 to -2.19)
Week 30 (n= 22, 13, 5, 10, 15, 8)	-4.36 (-5.83 to -2.90)	-2.23 (-4.28 to -0.18)	-1.20 (-2.82 to 0.42)	-4.20 (-5.66 to -2.74)
Week 36 (n= 23, 8, 3, 10, 11, 6)	-4.43 (-5.95 to -2.92)	-3.38 (-5.74 to -1.01)	-1.00 (-5.30 to 3.30)	-4.00 (-5.39 to -2.61)
Week 48 (n= 17, 6, 3, 8, 8, 6)	-5.47 (-6.64 to -4.30)	-3.33 (-6.49 to -0.17)	-1.00 (-7.57 to 5.57)	-4.13 (-6.67 to -1.58)
Week 60 (n= 9, 2, 2, 5, 5, 4)	-4.89 (-6.54 to -3.24)	-4.50 (-23.56 to 14.56)	-3.00 (-999 to 999)	-4.40 (-6.66 to -2.14)

Notes:

[104] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[105] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[106] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[107] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

End point values	UPA 15 mg/ABBV-105 placebo	Placebo in M16-063/ABBV-599 in M16-763		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17[108]	8[109]		
Units: units on a scale				
arithmetic mean (confidence interval 95%)				
Week 18 (n= 22, 15, 7, 10, 17, 8)	-5.29 (-6.54 to -4.05)	-2.38 (-4.65 to -0.10)		
Week 24 (n= 25, 14, 7, 10, 16, 8)	-4.88 (-6.43 to -3.32)	-3.50 (-5.50 to -1.50)		
Week 30 (n= 22, 13, 5, 10, 15, 8)	-4.53 (-5.75 to -3.32)	-3.13 (-5.55 to -0.70)		

Week 36 (n= 23, 8, 3, 10, 11, 6)	-5.55 (-6.80 to -4.29)	-3.00 (-6.18 to 0.18)		
Week 48 (n= 17, 6, 3, 8, 8, 6)	-5.38 (-7.10 to -3.65)	-3.67 (-6.90 to -0.44)		
Week 60 (n= 9, 2, 2, 5, 5, 4)	-4.80 (-7.19 to -2.41)	-3.00 (-5.25 to -0.75)		

Notes:

[108] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

[109] - Those who completed M16-063 and rcvd ≥ 1 dose of assigned study drug in M16-763 w/ available data

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality is reported from enrollment to the end of study; median time on follow-up was up to 337 days. TEAEs/SAEs were collected from the first dose in M16-763 until 30 days after last dose, up to 52 weeks.

Adverse event reporting additional description:

All-cause mortality and adverse events: all participants who completed Study M16-063 and received at least one dose of assigned study drug in Study M16-763, grouped according to treatments actually received in Study M16-763

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	ABBV-599 in M16-063/ABBV-599 in M16-763

Reporting group description:

60 mg elsubrutinib capsule once a day by mouth for 48 weeks; 15 mg film-coated upadacitinib tablet once a day by mouth for 48 weeks

Reporting group title	ABBV-105 60 mg/UPA placebo

Reporting group description:

60 mg elsubrutinib capsule once a day by mouth for 48 weeks; placebo film-coated tablet for upadacitinib once a day by mouth for 48 weeks

Reporting group title	ABBV-105 20 mg/UPA placebo

Reporting group description:

20 mg elsubrutinib capsule once a day by mouth for 48 weeks; placebo film-coated tablet for upadacitinib once a day by mouth for 48 weeks

Reporting group title	ABBV-105 5 mg/UPA placebo

Reporting group description:

5 mg elsubrutinib capsule once a day by mouth for 48 weeks; placebo film-coated tablet for upadacitinib once a day by mouth for 48 weeks

Reporting group title	UPA 15 mg/ABBV-105 placebo

Reporting group description:

15 mg film-coated upadacitinib tablet once a day by mouth for 48 weeks; placebo capsule for elsubrutinib once a day by mouth for 48 weeks

Reporting group title	Placebo in M16-063/ABBV-599 in M16-763

Reporting group description:

Placebo in M16-063; 60 mg elsubrutinib capsule once a day by mouth for 48 weeks and 15 mg film-coated upadacitinib tablet once a day by mouth for 48 weeks in M16-763

Serious adverse events	ABBV-599 in M16-063/ABBV-599 in M16-763	ABBV-105 60 mg/UPA placebo	ABBV-105 20 mg/UPA placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 28 (3.57%)	0 / 16 (0.00%)	0 / 12 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

LUNG ADENOCARCINOMA			
subjects affected / exposed	1 / 28 (3.57%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
PERIPROSTHETIC FRACTURE			
subjects affected / exposed	0 / 28 (0.00%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	ABBV-105 5 mg/UPA placebo	UPA 15 mg/ABBV-105 placebo	Placebo in M16-063/ABBV-599 in M16-763
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	1 / 20 (5.00%)	0 / 9 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
LUNG ADENOCARCINOMA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 20 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
PERIPROSTHETIC FRACTURE			
subjects affected / exposed	0 / 12 (0.00%)	1 / 20 (5.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	ABBV-599 in M16-063/ABBV-599 in M16-763	ABBV-105 60 mg/UPA placebo	ABBV-105 20 mg/UPA placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 28 (28.57%)	10 / 16 (62.50%)	3 / 12 (25.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

BASAL CELL CARCINOMA			
subjects affected / exposed	0 / 28 (0.00%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	0 / 28 (0.00%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 28 (0.00%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
DRUG INTOLERANCE			
subjects affected / exposed	0 / 28 (0.00%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
DRUG WITHDRAWAL SYNDROME			
subjects affected / exposed	0 / 28 (0.00%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 28 (0.00%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 28 (0.00%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
PYREXIA			
subjects affected / exposed	0 / 28 (0.00%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 28 (0.00%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
DEPRESSION			
subjects affected / exposed	0 / 28 (0.00%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Investigations			
URINE ANALYSIS ABNORMAL			

subjects affected / exposed	0 / 28 (0.00%)	0 / 16 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	0 / 28 (0.00%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	0 / 28 (0.00%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
HEADACHE			
subjects affected / exposed	0 / 28 (0.00%)	0 / 16 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
TREMOR			
subjects affected / exposed	0 / 28 (0.00%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 28 (0.00%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
MICROCYTIC ANAEMIA			
subjects affected / exposed	0 / 28 (0.00%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 28 (0.00%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
DIARRHOEA			
subjects affected / exposed	0 / 28 (0.00%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
NAUSEA			
subjects affected / exposed	0 / 28 (0.00%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
VOMITING			
subjects affected / exposed	1 / 28 (3.57%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	1	1	0

Skin and subcutaneous tissue disorders			
DERMATITIS			
subjects affected / exposed	0 / 28 (0.00%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
RENAL CYST			
subjects affected / exposed	1 / 28 (3.57%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
JOINT SWELLING			
subjects affected / exposed	0 / 28 (0.00%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
RHEUMATOID ARTHRITIS			
subjects affected / exposed	2 / 28 (7.14%)	4 / 16 (25.00%)	0 / 12 (0.00%)
occurrences (all)	2	4	0
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	1 / 28 (3.57%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
EAR INFECTION			
subjects affected / exposed	0 / 28 (0.00%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
GASTROENTERITIS			
subjects affected / exposed	0 / 28 (0.00%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
NASOPHARYNGITIS			
subjects affected / exposed	0 / 28 (0.00%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
ORAL CANDIDIASIS			
subjects affected / exposed	0 / 28 (0.00%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
RESPIRATORY TRACT INFECTION VIRAL			
subjects affected / exposed	0 / 28 (0.00%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
TOOTH INFECTION			

subjects affected / exposed	0 / 28 (0.00%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	3 / 28 (10.71%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	3	1	0
URETHRITIS			
subjects affected / exposed	0 / 28 (0.00%)	0 / 16 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 28 (3.57%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
DIABETES MELLITUS			
subjects affected / exposed	0 / 28 (0.00%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 28 (0.00%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	ABBV-105 5 mg/UPA placebo	UPA 15 mg/ABBV-105 placebo	Placebo in M16-063/ABBV-599 in M16-763
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 12 (41.67%)	7 / 20 (35.00%)	3 / 9 (33.33%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BASAL CELL CARCINOMA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 20 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 20 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 20 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
DRUG INTOLERANCE			

subjects affected / exposed	0 / 12 (0.00%)	1 / 20 (5.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
DRUG WITHDRAWAL SYNDROME			
subjects affected / exposed	0 / 12 (0.00%)	0 / 20 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 20 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 20 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PYREXIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 20 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 12 (0.00%)	0 / 20 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
DEPRESSION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 20 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Investigations			
URINE ANALYSIS ABNORMAL			
subjects affected / exposed	0 / 12 (0.00%)	0 / 20 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	0 / 12 (0.00%)	1 / 20 (5.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 20 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
HEADACHE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 20 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

TREMOR			
subjects affected / exposed	0 / 12 (0.00%)	0 / 20 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 20 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
MICROCYTIC ANAEMIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 20 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 20 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
DIARRHOEA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 20 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
NAUSEA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 20 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
VOMITING			
subjects affected / exposed	0 / 12 (0.00%)	0 / 20 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
DERMATITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 20 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
RENAL CYST			
subjects affected / exposed	0 / 12 (0.00%)	1 / 20 (5.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
JOINT SWELLING			
subjects affected / exposed	1 / 12 (8.33%)	0 / 20 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
RHEUMATOID ARTHRITIS			

subjects affected / exposed	0 / 12 (0.00%)	0 / 20 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	0 / 12 (0.00%)	1 / 20 (5.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
EAR INFECTION			
subjects affected / exposed	0 / 12 (0.00%)	1 / 20 (5.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
GASTROENTERITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 20 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
NASOPHARYNGITIS			
subjects affected / exposed	0 / 12 (0.00%)	1 / 20 (5.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
ORAL CANDIDIASIS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 20 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
RESPIRATORY TRACT INFECTION VIRAL			
subjects affected / exposed	0 / 12 (0.00%)	1 / 20 (5.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
TOOTH INFECTION			
subjects affected / exposed	0 / 12 (0.00%)	1 / 20 (5.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 12 (8.33%)	1 / 20 (5.00%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
URETHRITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 20 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 12 (0.00%)	2 / 20 (10.00%)	1 / 9 (11.11%)
occurrences (all)	0	2	1
Metabolism and nutrition disorders			

DIABETES MELLITUS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 20 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 20 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 October 2018	Version 2 -- Added the following for additional safety monitoring for potential AEs, clarification of clinical definitions, and to assure compliance with local guidelines: -- 12-lead electrocardiogram (ECG) at Weeks 12, 18, 24, 30, and 48; -- Clarification of the rationale/objective for exploratory biomarker research; -- Added contraception barrier method as a requirement per local regulations; -- Added guidance regarding unblinding in event of a medical situation requiring urgent clinical need to know randomization assignment; and -- Added information regarding subject at-home weekly temperature monitoring for assessment of serious infections
17 January 2019	Version 3 -- Added advisement to follow local public health guidelines for management of potential TB risk -- Added T SPOT TB test as possible test for identification of latent TB -- Added an UPA efficacy analysis set -- Added the following for additional safety monitoring for potential AEs, clarification of clinical definitions, and to assure compliance with local guidelines: -- 12-lead ECG at Weeks 12, 18, 24, 30, and 48; -- Clarification of the rationale/objective for exploratory biomarker research; -- Added contraception barrier method as a requirement per local regulations; and -- Added guidance regarding unblinding in event of a medical situation requiring urgent clinical need to know randomization assignment -- Added information regarding subject at-home weekly temperature monitoring for assessment of serious infections -- Added information regarding UPA safety data -- Clarified safety endpoints regarding Data Monitoring Committee and when the clinical trial would be discontinued -- Updated eligibility criteria to include relevant eligibility requirements from Study M16-063 applicable to Study M16-763 -- Updated efficacy endpoints and statistical analysis for efficacy to reflect that there were no primary efficacy endpoints and that no formal statistical tests would be applied -- Clarified that the use of live vaccines was to be avoided for 4 weeks after the last dose of study drug for alignment with Study M16-063
06 February 2020	Version 4 -- Added additional Clinical Disease Activity Index (CDAI) efficacy endpoints -- Clarified birth control practices in eligibility criteria -- Clarified study discontinuation criteria, study drug discontinuation processes, study drug dispensation instructions, and herpes zoster vaccine instructions -- Added information to clarify Safety Analysis Set parameters -- Added an All ABBV-599 efficacy analysis set (Group 7: Group 1 and Group 6 combined) -- Added an interim analysis to review long-term safety and efficacy -- Removed troponin and troponin + creatine kinase myocardial band (CKMB) testing (asymptomatic creatine phosphokinase [CPK] elevation is a known Janus kinase [JAK] inhibitor class effect) -- Removed reference to liver biopsies as there were no liver biopsies at Screening or any time during the Study

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported